



App. No. 10/728,442

Amdt. dated April 27, 2005

Reply to Office Action of October 27, 2004

PATENT

**Amendments to the Claims:**

Please cancel claims 1-31 and add new claims 32-81. This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1 1-31 (canceled)

1 32 (new): A mass spectrometry probe comprising:

2 (a) a sample presenting surface, wherein the sample presenting surface is a  
3 surface of the probe;

4 (b) energy absorbing molecules immobilized by chemical bonding to the  
5 sample presenting surface; and

6 (c) an affinity reagent immobilized by chemical bonding to the sample  
7 presenting surface, wherein the energy absorbing molecules are different  
8 from the affinity reagent.

1 33 (new): The probe of claim 32, wherein the sample presenting surface does not  
2 have additional matrix molecules.

1 34 (new): The probe of claim 32, wherein the probe comprises metal.

1 35 (new): The probe of claim 32, wherein the energy absorbing molecules are  
2 covalently bound to the sample presenting surface.

1 36 (new): The probe of claim 32, wherein the energy absorbing molecules and  
2 affinity reagent are arranged on the sample presenting surface in a predetermined array.

1                   37 (new): The probe of claim 32, wherein the energy absorbing molecules are  
2 selected from the group consisting of dimethoxy hydroxycinnamic acid, cinnamamide, cinnamyl  
3 bromide, dihydroxybenzoic acid, and cyanohydroxycinnamic acid.

1                   38. (new): The probe of claim 32, wherein the affinity reagent is covalently  
2 bound to the sample presenting surface.

1                   39. (new): The probe of claim 32, wherein the affinity reagent is selected from  
2 the group consisting of a metal ion, a protein, a peptide, a nucleic acid and a dye.

1                   40. (new): The probe of claim 39, wherein the affinity reagent comprises a metal  
2 ion.

1                   41. (new): The probe of claim 40, wherein the metal ion is selected from copper  
2 or iron.

1                   42. (new): The probe of claim 39, wherein the affinity reagent comprises a  
2 protein or peptide.

1                   43 (new): The probe of claim 42, wherein the protein or peptide is an  
2 immunoglobulin.

1                   44 (new): The probe of claim 39, wherein the affinity reagent comprises a  
2 nucleic acid.

1                   45 (new): The probe of claim 44, wherein the nucleic acid is DNA.

1                   46 (new): The probe of claim 32, wherein the analyte comprises a protein.

1                   47 (new): The probe of claim 32, wherein the analyte comprises a nucleic acid.

1                   48 (new): The probe of claim 32, wherein the analyte is bound to the affinity  
2 reagent.

1                   49 (new): A method for detecting an analyte comprising:

- 2                   (a)     capturing an analyte on a sample presenting surface of a mass  
3                   spectrometry probe, wherein the sample presenting surface is a surface of  
4                   the probe, wherein the probe comprises (i) energy absorbing molecules  
5                   immobilized by chemical bonding to the sample presenting surface, (ii) an  
6                   affinity reagent immobilized by chemical bonding to the sample  
7                   presenting surface, wherein the energy absorbing molecules are different  
8                   from the affinity reagent, wherein the analyte is not dispersed in a matrix  
9                   crystalline structure, but is presented within, on or above the energy  
10                  absorbing molecules; and  
11                  (b)     detecting the captured analyte by laser desorption/ionization mass  
12                  spectrometry.

1                   50.     The method of claim 49, wherein additional matrix molecules are not  
2 added.

1                   51 (new): The method of claim 49, wherein the energy absorbing molecules are  
2 covalently bound to the sample presenting surface.

1                   52 (new): The method of claim 49, wherein the energy absorbing molecules and  
2 affinity reagent are arranged on the sample presenting surface in a predetermined array.

1                   53 (new): The method claim 49, wherein the energy absorbing molecules are  
2 selected from the group consisting of dimethoxy hydroxycinnamic acid, cinnamamide, cinnamyl  
3 bromide, dihydroxybenzoic acid, and cyanohydroxycinnamic acid.

1                   54. (new): The method of claim 49, wherein the affinity reagent is covalently  
2 bound to the sample presenting surface.

1                   55. (new): The method of claim 49, wherein the affinity reagent is selected from  
2 the group consisting of a metal ion, a protein, a peptide, a nucleic acid and a dye.

1                   56. (new): The method of claim 55, wherein the affinity reagent comprises a  
2 metal ion selected from copper or iron.

1                   57. (new): The method of claim 55, wherein the affinity reagent comprises an  
2 immunoglobulin.

1                   58 (new): The method of claim 55, wherein the affinity reagent comprises DNA.

1                   59 (new): The method of claim 49, wherein the sample is selected from the  
2 group consisting of blood, tears, urine, saliva, gastrointestinal fluids, spinal fluid, amniotic fluid,  
3 bone marrow, bacteria, viruses, cells in culture, biopsy tissue, plant tissue or fluids and insect  
4 tissue or fluids.

1                   60 (new): The method of claim 49, wherein the analyte comprises a protein.

1                   61 (new): The method of claim 49, wherein the analyte comprises a nucleic acid.

1                   62 (new): The method of claim 61, wherein the nucleic acid is DNA.

1                   63 (new): A mass spectrometry apparatus comprising:

2                   (a) a probe comprising:

3                   i. a sample presenting surface;

4                   ii. energy absorbing molecules immobilized by chemical bonding to  
5 the sample presenting surface;

- 6                           iii.     an affinity reagent capable of binding an analyte immobilized by  
7   chemical bonding to the sample presenting surface; and  
8                           iv.     an analyte that is not dispersed in a matrix crystalline structure, but  
9   is presented within, on or above the energy absorbing molecules,  
10    wherein the energy absorbing molecules are different from the  
11    affinity reagent;  
12                   (b)     an energy source that directs laser energy to the sample presenting surface  
13    for desorbing and ionizing the analyte;  
14                   (c)     a detector that detects the desorbed, ionized analyte  
15                   (d)     a spectrometer tube into which ionized analyte is accelerated;  
16                   (e)     means for applying an accelerating electrical potential to the desorbed,  
17    ionized analyte; wherein the mass spectrometer is a time-of-flight mass  
18    spectrometer; and  
19                   (f)     vacuum means for applying a vacuum to the interior of the tube.

1                   64.     The probe of claim 63, wherein the sample presenting surface does not  
2     have additional matrix molecules.

1                   65 (new): The apparatus of claim 63, wherein the detector comprises an electron  
2     multiplier.

1                   66 (new): The apparatus of claim 63, wherein the energy source is energy from a  
2     nitrogen laser or an Nd-YAG laser.

1                   67 (new): The apparatus of claim 63, wherein the energy absorbing molecules  
2     are noncovalently bound to the sample presenting surface.

1                   68 (new): The apparatus of claim 63, wherein the energy absorbing molecules  
2     are covalently bound to the sample presenting surface.

1                    69 (new): The apparatus of claim 63, wherein the energy absorbing molecules  
2 are selected from the group consisting of dimethoxy hydroxycinnamic acid, cinnamamide,  
3 cinnamyl bromide, dihydroxybenzoic acid, and cyanohydroxycinnamic acid.

1                    70. (new): The apparatus of claim 63, wherein the affinity reagent is  
2 noncovalently bound to the sample presenting surface.

1                    71. (new): The apparatus of claim 63, wherein the affinity reagent is covalently  
2 bound to the sample presenting surface.

1                    72. (new): The apparatus of claim 63, wherein the affinity reagent is selected  
2 from the group consisting of a metal ion, a protein, a peptide, a nucleic acid and a dye.

1                    73. (new): The apparatus of claim 72, wherein the affinity reagent comprises a  
2 metal ion.

1                    74. (new): The apparatus of claim 73, wherein the metal ion is selected from  
2 copper or iron.

1                    75. (new): The apparatus of claim 72, wherein the affinity reagent comprises a  
2 protein or peptide.

1                    76 (new): The apparatus of claim 75, wherein the protein or peptide is an  
2 immunoglobulin.

1                    77 (new): The apparatus of claim 72, wherein the affinity reagent comprises a  
2 nucleic acid.

1                    78 (new): The apparatus of claim 77, wherein the nucleic acid is DNA.

1                    79 (new): The apparatus of claim 63, wherein the analyte comprises a protein.

1                   80 (new): The apparatus of claim 63, wherein the analyte comprises a nucleic  
2 acid.

1                   81 (new): The apparatus of claim 80, wherein the nucleic acid is DNA.